

REMARKS/ARGUMENTS

Claims 1, 4, 16-18, 20-26 and 28-30 are pending in this matter. Claims 23-26 and 28-30 have been allowed. Claims 1, 4, 16-18 and 20-22 remain rejected; however, in view of the remarks and Declaration included herein, Applicants submit that the remaining claims are also allowable. Reconsideration is respectfully requested.

I. REJECTIONS UNDER 35 U.S.C. § 102(a)

Claims 1, 4, and 16-20 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Ahmad *et al.*, *Gastroenterology*, Vol. 122, pages 854-866 (Ahmad *et al.*, April 2002). In addition, claims 1, 4, and 16-20 were also rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Radlmayr *et al.*, *Gastroenterology*, Vol. 122, No. 7 pages 2091-2095 (June, 2002). In response, Applicants respectfully traverse the rejection.

The present application, U.S. Application No. 10/526,256 (“the ‘256 application”), is a national phase application arising from PCT Application No. PCT/03/023,926, (“PCT ‘926”) filed July 30, 2003. The PCT ‘926 application claims priority to U.S. Provisional Application No. 60/407,391, filed August 30, 2002 and U.S. Application No. 10/356,736, filed January 30, 2003.

As U.S. Provisional Application No. 60/407,391 was filed on August 30, 2002, Ahmad *et al.* (April 2002) and Radlmayr *et al.* (June 2002) are considered by the Examiner to be 35 U.S.C. § 102(a) art.

A. Abreu *et al.*

Abreu *et al.*, *Gastroenterology*, Volume 123, Issue 3, pages 679-688 (2002) (“the Abreu *et al.* Vol. 123 reference, Sept 2002”) was published in September 2002 and embodies the claimed invention. The September 2002 date is verified by Exhibit 1, which is a copy of the “Table of Contents” from Volume 123, Issue 3 of the journal *Gastroenterology*. In order for the Abreu *et al.* Vol. 123 reference Sept 2002 to have been published in the September issue of 2002, it must have been received by the journal **before** September 2002.

In fact, it is clear from the Abreu *et al.*, Volume 123, reference on page 688, right hand column in the footnotes, that the manuscript (preprint) was received by the journal on **February 8, 2002**. February 8, 2002 **predates** both Ahmad *et al.* (April 2002) as well as Radlmayr *et al.* (June 2002).

The currently claimed rejected subject matter is embodied in the Abreu *et al.* Vol. 123 reference. The date of receipt of the manuscript by the journal *Gastroenterology* clearly antedates Ahmad *et al.* (April 2002) as well as Radlmayr *et al.* (June 2002).

B. 37 CFR § 1.131 Declaration by the Inventors

Applicants submit herewith a Declaration ("Declaration") under 37 CFR § 1.131, signed by each of the named inventors evidencing prior invention in the United States before the effective dates of each of the references. The Declaration has attached Exhibits A & B. Paragraphs 4-6 of the enclosed Declaration are reproduced below for the convenience of the Examiner and recite as follows:

4. Attached Exhibit A is a journal article that embodies the currently claimed invention. The journal article is entitled, "Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease, by Maria T. Abreu, *et al.*, pages 679-688, Volume 123, Issue 3, (September 2002).

5. The Table of Contents of this September 2002 journal issue is attached as Exhibit B.

6. These Exhibits provide evidence of the conception of the invention and its reduction to practice. A manuscript, from which this journal article arose, was prepared prior to February 8, 2002. This is clear from the footnote on page 688 of the journal article, which states that the manuscript was received by the publisher on February 8, 2002.

Under MPEP § 715.07 it states:

The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the

fact. FACTS, not conclusions, must be alleged. Evidence in the form of exhibits may accompany the affidavit or declaration. Each exhibit relied upon should be specifically referred to in the affidavit or declaration, in terms of what it is relied upon to show. [Emphasis added].

Applicants have provided the essential thing to show priority of invention. The date of the *declared* submission of the manuscript in the journal coupled with the date of publication of the article in the journal is satisfactory evidence of prior invention. Each of the inventors declares in paragraph 6:

...A manuscript, from which this journal article arose, was prepared prior to February 8, 2002.

Their declaration is corroborated by the journal itself by the footnote which recites: "Received February 8, 2002. Accepted March 16, 2002." In other words, according to the Declaration, a manuscript was prepared before February 8, 2002 and submitted to the journal for publication. The journal later published the manuscript in September 2002 and memorialized the date of receipt of the original manuscript as is customary and normal business practice. An actual copy of the manuscript is not required as the journal article itself is a facsimile of the accepted manuscript. The date of March 16, 2002 is the date of the actual acceptance of the manuscript by the journal, which date still predates the effective dates of either of the references.

C. The Documentary Evidence Clearly Shows a Date *Prior* to the Effective Date of the References

The Declaration and exhibits clearly state facts and evidence a date of invention in this country prior to the effective date of the cited references. When all the evidence is viewed in its entirety, including the Declaration, the Exhibits and later publication, Applicants' evidence clearly and convincingly establishes a date of invention prior to February 8, 2002. This date antedates the cited references.

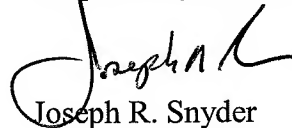
D. A Timeline of Events

Applicants have included a timeline of events as Exhibit 2 for the convenience of the Examiner. As shown therein, Applicants were clearly in possession of the invention prior to the publication of Ahmad *et al.* (April 2002) and Radlmayr *et al.* (June 2002).

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Joseph R. Snyder
Reg. No. 39,381

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Gastroenterology

Volume 123, Issue 3, Pages 661-958 (September 2002)

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Joseph H. Sellin

pages 661-662

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Gastroenterology News

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Leslie Lang

page 663

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NIH set to expand digestive diseases study section

Leslie Lang

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Leslie Lang

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Leslie Lang

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Lloyd Mayer

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Clinical-Alimentary Tract

Paradoxical coexpression of proinflammatory and down-regulatory cytokines in intestinal T cells in childhood celiac disease

Göte Forsberg*,†, Olle Hemell†, Silvia Melgar*, Anne Israelsson*, Sten Hammarström*, Marie-Louise Hammarström*

pages 667-678

☐ Abstract | [Full Text](#) | [Full-Text PDF \(306 KB\)](#)

Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease

Maria T. Abreu, Kent D. Taylor, Ying-Chao Lin, Tieu Hang, Joanne Galennie, Carol J. Landers, Eric A. Vasilias, Lori Y. Kam, Micha

Rojany, Konstantinos A. Papadakis, Jerome I. Rotter, Stephan R. Targan, Huiying Yang

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☐ Abstract | [Full Text](#) | [Full-Text PDF \(141 KB\)](#)

Selected loss of tolerance evidenced by Crohn's disease-associated immune responses to auto- and microbial antigens

Carol J. Landers, Offer Cohavy, Rajeev Misra, Huiying Yang, Ying-Chao Lin, Jonathan Braun, Stephan R. Targan

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Biographical Sketch

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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(108 KB\)](#)**Predictors of response to infliximab in patients with Crohn's disease**


Mansour A. Parsi, Jean-Paul Achkar, Scott Richardson, Jeffry Katz, Jeffrey P. Hammel, Bret A. Lashner, Aaron Brzezinski

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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(92 KB\)](#)**Uveitis and erythema nodosum in inflammatory bowel disease: Clinical features and the role of HLA genes**

Timothy R. Orchard, C.N. Chua, Tariq Ahmad, Hung Cheng, Kenneth I. Welsh, Derek P. Jewell


pages 714-718

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(97 KB\)](#)**Clinical-Liver, Pancreas, and Biliary Tract****Determinants of early mortality in patients with decompensated chronic hepatitis B treated with antiviral therapy**

Robert J. Fontana, Hie-Won L. Hann, Robert P. Perrillo, John M. Vierling, Theresa Wright, Jorge Rakela, Gaya Anshuetz, Randy Davis,


Stephen D. Gardner, Nathaniel A. Brown

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Gin-Ho Lo, Wen-Chi Chen, Mei-Hsiu Chen, Ping-I Hsu, Chiun-Ku Lin, Wei-Lun Tsai, Kwok-Hung Lai


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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(116 KB\)](#)**Primary prophylaxis of variceal hemorrhage: A randomized controlled trial comparing band ligation, propranolol, and isosorbide mononitrate**

Hock F. Lui, Adrian J. Stanley, Ewan H. Forrest, Rajiv Jalan, W. Stuart Hislop, Peter R. Mills, Niall D.C. Finlayson, Alastair J. Macgillchrist,

Peter C. Hayes

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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(104 KB\)](#)**The utility of radiological imaging in nonalcoholic fatty liver disease**

Sherif Saadeh*, Zobair M. Younossi*,†, Erick M. Remer\$, Terry Gramlich□, Janus P. Ong†, Maja Hurley\$, Kevin D. Mullen*, James N.

Cooper†, Michael J. Sheridan†

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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(80 KB\)](#)**Basic-Alimentary Tract****The APC tumor suppressor controls entry into S-phase through its ability to regulate the cyclin D/RB pathway**

Christopher D. Heinen, Kathleen Heppner Goss, James R. Cornelius, George F. Babcock, Erik S. Knudsen, Timothy Kowalik, Joanna

Grodén

pages 751-763

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(407 KB\)](#)**JunD stabilization results in inhibition of normal intestinal epithelial cell growth through P21 after polyamine depletion**


Li Li*,†, Lan Liu*,†, Jaladanki N. Rao*,†, Ali Esmaili*, Eric D. Strauch*, Barbara L. Bass*,†, Jian-ying Wang*,†,§

pages 764-779

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(1023 KB\)](#)**Fas/CD95 is required for gastric mucosal damage in autoimmune gastritis**


Aiden C.J. Marshall, Frank Alderuccio, Ban-Hock Toh

pages 780-789

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(592 KB\)](#)**HMGB1 B box increases the permeability of Caco-2 enterocytic monolayers and impairs intestinal barrier function in mice**

Penny L. Sappington*, Runkuan Yang*, Huan Yang†, Kevin J. Tracey†, Russell L. Delude*,§, Mitchell P. Fink*,□

pages 790-802

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(278 KB\)](#)**Celiac lesion T cells recognize epitopes that cluster in regions of gliadins rich in proline residues**

Helene Arentz-Hansen, Stephen N. Mcadam, Øyvind Molberg, Burkhard Fleckenstein, Knut E.A. Lundin, Thomas J.D. Jørgensen,

Günther Jung, Peter Roepstorff, Ludvig M. Sollid

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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(130 KB\)](#)**The type of sodium-coupled solute modulates small bowel mucosal injury, transport function, and ATP after ischemia/reperfusion injury in rats**

Rosemary A. Kozar*, Stanley G. Schultz†, Heitham T. Hassoun*, Roland Desoigne*, Norman W. Weisbrodt†, Marian M. Haber□,

Frederick A. Moore*

pages 810-816

 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(333 KB\)](#)**Expression of human intestinal mucin is modulated by the β-galactoside binding protein galectin-3 in colon cancer**


Steven P. Dudas, Christopher K. Yunker, Lawrence R. Sternberg, James C. Byrd, Robert S. Bresalier

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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(1594 KB\)](#)**Coupling of M₂ muscarinic receptor to L-type Ca²⁺ channel via c-src kinase in rabbit colonic circular smooth muscle**


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 [Abstract](#) | [Full Text](#) | [Full-Text PDF \(172 KB\)](#)**Basic-Liver, Pancreas, and Biliary Tract****Hepcidin expression inversely correlates with the expression of duodenal iron transporters and iron absorption in rats**

David M. Frazer, Sarah J. Wilkins, Erika M. Becker, Christopher D. Vulpe, Andrew T. Mckie, Deborah Trinder, Gregory J. Anderson


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
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Scott A. Cely

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Reply

Alexander Swidsinski

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Answer to the image of the month question (page 666): Pyogenic liver abscess complicated by bronchial fistula


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
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
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EXHIBIT 2

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